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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/183,055	10/29/1998	CARL H. JUNE	36119-125US8	2710

7590 07/18/2005
Colleen Superko Esq
Hale and Dorr LLP
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Boston, MA 02109

EXAMINER

GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 07/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/183,055

Applicant(s)

JUNE ET AL.

Examiner

Phillip Gambel

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 69, 70 and 72 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 69, 70, 72 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- 1) ☐ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission, filed on 7/29/04, has been entered.

Applicant's amendment, filed 7/29/04, has been entered.

Claim 69 has been amended.

Claims 1-68 and 71 have been canceled previously.

Claims 69, 70 and 72 are pending and under consideration in the instant application.

2. Applicant's submission of pending USSNs on the IDS, filed 12/2/04, is acknowledged, however these citations have been lined through as they are not appropriate for printing on the face of an U.S. patent.

3. Applicant's Petitions Under 37 CFR 1.182 To Withdraw A Record Terminal Disclaimer, filed 7/24/04 and 8/13/04, are acknowledged. 7/24/04 *ju*

After the mailing of this Office Action, the instant application will be forwarded to the Office of Petitions to consider said Petitions.

The examiner apologizes for any inconvenience to applicant in this matter.

4. In view of applicant's Petition to Correct Inventorship Under 37 CFR 1.48(b), filed 8/13/04; the inventorship in this nonprovisional application has been changed by the deletion of Thompson and Nabel from the list of co-inventors.

The inventors of the claimed invention are June, Rennert, Gray and Freeman.

5. Upon the change of inventorship indicated above and applicant's statement in the Supplemental Petition under 37 CFR 1.182 To Withdraw A Record Terminal Disclaimer, the following is set forth.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(f) he did not himself invent the subject matter sought to be patented

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7. Claims 69, 70 and 72 are rejected under 35 U.S.C. § 102(f) because the applicants did not invent the claimed subject matter.

Upon the change of inventorship indicated above and applicant's statement in the Supplemental Petition under 37 CFR 1.182 To Withdraw A Record Terminal Disclaimer;
the inventorship as well as the ownership of the instant application differs from that of U.S. Patent No. 5,858,358.

Applicant asserts that the pending and the patented claims are not obvious over one another in that the instant application is directed to a method of stimulating CD8⁺ T cell with a population of T cell to proliferate, comprising contacting a population of T cells with an anti-CD3 antibody, anti-CD28 antibody and an anti-CD9 antibody,
while the patented claims do not recite anti-CD28 antibody.

Applicant further asserts that there is simply no disclosure in the claims of U.S. Patent NO. 5,858,358 to stimulate a population of cells with an anti-CD3 antibody, anti-CD9 and an anti-CD28 antibody.

Applicant submits that the ordinary artisan would readily appreciate that the claims of the instant application and U.S. Patent NO. 5,858,358 are different and not obvious over one another.

First of all, it is noted that a Terminal Disclaimer has been filed and recorded with respect to the instant application and U.S. Patent No. 5,858,358.

Although applicant has filed a Petition and a Supplemental Petition to withdraw the previously recorded Terminal Disclaimer, a decision on these Petitions has not been determined at this time.

Therefore, the record stands currently that the instant claims and the patented claims are obvious in view of the submission of the Terminal Disclaimer in response to the previous rejection of obvious double patenting.

While it is agreed that the instant claims recite anti-CD28 antibodies in addition to the common recitation of anti-CD3 antibodies and anti-CD9 antibodies between the instant and patented methods,

the ordinary artisan at the time the invention was made readily employed the combination of anti-CD3 antibodies and anti-CD28 antibodies to activate lymphocytes, including cytotoxic CD8⁺ T cells for immunotherapy,

as evidenced by Ledbetter et al. (EP 0440373 A1; see entire document, including the Abstract, Summary of the Invention, Detailed Description of the Invention and Claims) (149; #A1).

For example, Ledbetter et al. teach that aggregating CD28 maximizes the cytolytic response (e.g., see Summary of the Invention).

At the time the invention was made, the ordinary artisan readily appreciated that anti-CD28 antibodies maximized the stimulation of T cells, including cytolytic CD8⁺ T cells that have been stimulated via CD3.

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Given this art known practice at the time the invention was made, the ordinary artisan would have been motivated to apply the combination of anti-CD3 and anti-CD28 antibodies to stimulate T cells, including CD8⁺ T cells to generate sufficient numbers of T cells for adoptive immunotherapy as well as to maximize the activity of these cells.

While the recitation of anti-CD9 antibodies in the instant and patented claims appears free of the prior art in the stimulation of T cell populations at the time the invention was made, the ordinary artisan was motivated to combine anti-CD3 and anti-CD28 antibodies to stimulate T cells in order to generate large numbers of cells and to maximize the function of said T cells, as known and practiced at the time the invention was made.

In contrast to applicant's assertions, combining anti-CD3 and anti-CD28 antibodies in stimulating T cells was a generally accepted principle at the time the invention was made.

Further, the instant disclosure supports the claimed methods of both the instant application and U.S. Patent No. 5,858,358. For example, it may be necessary to reactivate and restimulate the T cells with anti-CD3 antibody and anti-CD28 antibodies for inducing long term stimulation of T cells (e.g. see page 14, paragraph 1 of the instant specification).

Because of this ambiguity, it is incumbent on applicants to provide a satisfactory showing which would lead to a reasonable conclusion that applicants alone are the inventors of the claimed invention.

To resolve the ambiguity, applicants may file a declaration by the non-applicants Thompson and Nabel or a declaration by applicant setting forth the facts which provide an explanation as to why the non-applicants Thompson and Nabel are not inventors.

The Petition to Correct Inventorship Under 37 CFR 1.48(b), filed 8/13/04, notes that the inventive subject matter of Thompson and Nabel is no longer being claimed in the instant application

However, Thompson and Nabel are co-inventors of the U.S. Patent No. 5,538,328, the subject of the previous double patenting rejection and terminal disclaimer of record.

Given the difference between the instant and patented claims is mainly drawn to the recitation of "anti-CD28 antibodies", while the patented claims do not recite these antibodies and given the contribution of Thompson and Nabel to the combination of anti-CD9 and anti-CD3 antibodies in the claimed methods,

a declaration by applicant setting forth the facts which provide an explanation as to why the non-applicants Thompson and Nabel are no longer co-inventors in view of the known use and practice to combine anti-CD28 antibodies with anti-CD3 antibodies to generate therapeutic amounts as well as to maximize the activity of T cells at the time the invention was made.

8. No claim is allowed.

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9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
March 30, 2005